

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
125293

REMS

BLA 125293
KRYSTEXXA™ (pegloticase)
PEGylated uric acid specific enzyme

Savient Pharmaceuticals, Inc.

One Tower Center Blvd.

East Brunswick, NJ 08816

Telephone: 732-565-4647

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS:

The goals of the KRYSTEXXA Risk Evaluation and Mitigation Strategy (REMS) are:

1. To inform healthcare providers about anaphylaxis, infusion reactions, and contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.
2. To inform patients about the serious risks associated with use of KRYSTEXXA.

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with KRYSTEXXA prescription in accordance with 21 CFR 208.24.

See the approved Medication Guide in Attachment A.

B. Communication Plan

Savient Pharmaceuticals, Inc. will implement a communication plan to healthcare providers to support implementation of this REMS.

Savient Pharmaceuticals, Inc. will institute a communication plan for healthcare providers who are expected to be the predominant healthcare providers who prescribe, administer and dispense KRYSTEXXA.

This communication plan is focused upon those physicians who actually will be responsible for patient interactions associated with the potential infusions of KRYSTEXXA. Due to the tight product distribution through Specialty Distributors and Specialty Pharmacies we have the ability to follow new product purchasers down to the physician and infusion centers where care will be provided.

We plan to provide new prescribers or new infusion centers the Dear Healthcare Provider (DHCP) or Dear Infusion Site Medical Personnel (DISMP) Letter, as appropriate, through this channel at the time the product is purchased or shipped to ensure those who prescribe, administer and dispense KRYSTEXXA receive these materials.

The communication plan will disseminate risk information about anaphylaxis and infusion reactions, and the contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.

Elements of the communication plan are:

1. A Dear Healthcare Provider Letter (see Attachment B) will be distributed to rheumatologists, nephrologists, and internists and family practice physicians, associated with infusion centers where KRYSTEXXA may be prescribed, administered and dispensed. This letter will be distributed by mail and electronically at product launch or within 60 days of KRYSTEXXA approval, whichever is sooner. The Dear Healthcare Provider Letter will be mailed and distributed electronically via e-mail again to these audiences once per year for an additional 2 years. In addition, for 2 years after launch, any known new prescribers of KRYSTEXXA not previously targeted will also be sent the Dear Healthcare Provider Letter. Savient will initially target approximately 5,000 rheumatologists, 7,500 nephrologists, and those internists and family practice physicians who purchase infused biologics from the Specialty Distributors or Specialty Pharmacies that Savient contracts with for product distribution. New prescribers purchasing KRYSTEXXA from these Specialty Distributors or Specialty Pharmacies will also receive the most recent Dear Healthcare Provider Letter and will be receiving letters annually as per the timeline in the communication plan. The targeted healthcare providers will be identified as follows: rheumatologists – American College of Rheumatology membership cross-referenced to the AMA database, nephrologists - American Society of Nephrology membership cross-referenced to the AMA database and Specialty Distributor databases. New prescribers will be identified using the Specialty Distributor and Specialty Pharmacy databases.

The approved Full Prescribing Information and a copy of the Medication Guide will also be distributed with this letter.

The DHCP Letter will also be available through a REMS-dedicated link from the www.KRYSTEXXA.com website. (See attached web page in Attachment C). Only FDA approved materials will be included on the REMS dedicated website.

2. A Dear Infusion Site Medical Personnel (DISMP) Letter (see Attachment D) will be distributed to directors or responsible heads of infusion sites engaged in the administration of rheumatologic infusions. This will be distributed by mail and electronically at product launch or within 60 days of KRYSTEXXA approval, whichever is sooner. The Dear Infusion Site Medical Personnel letter will be mailed and distributed electronically via e-mail again to this audience once per year for an additional 2 years. Savient will initially target all infusion sites (approximately 1,500 infusion sites) which will be identified using the customer lists of infusion centers from the databases of Specialty Distributors and Specialty Pharmacies. In addition, for 2 years after launch, any known new infusion sites for administration of KRYSTEXXA not previously targeted will also be sent the Dear Infusion Site Medical Personnel Letter.

The approved prescribing information and a copy of the Medication Guide will also be distributed with this letter.

The DISMP Letter will also be available through a REMS-dedicated link from the www.KRYSTEXXA.com website. (See attached web page in Attachment C). Only FDA approved materials will be included on the REMS dedicated website.

3. Savient will distribute Dear Healthcare Provider Letter, Prescribing Information, and Medication Guide at the American College of Rheumatology, American College of Physicians, and the American Society of Nephrology annual meetings. The Dear Infusion Site Medical Personnel Letter, Prescribing Information, and Medication Guide will be distributed at the Infusion Nurses Society Annual Meeting. This effort will start at the first annual meeting post-approval of the REMS, provided the deadlines for processing requests through the respective organizations have not passed (in which case the non-promotional materials will be distributed at the next annual meeting).
4. Savient will publish, within 90 days of product approval, journal information pieces about risks of anaphylaxis, infusion reactions, and the contraindicated use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency, with key aspects of management. These announcements will appear in the following professional societies' journals: American College of Rheumatology, American College of Physicians, the American Society of Nephrology and the Infusion Nurses Society.
 - Arthritis and Rheumatism – Official monthly journal of the American College of Rheumatology.
 - Annals of Internal Medicine – Official monthly journal of the American College of Physicians
 - Journal of the American Society of Nephrology – Official monthly journal of American Society of Nephrology.
 - Journal of Infusion Nursing – Official bi-monthly journal of the Infusion Nurses Society

These announcements will be published on a twice-yearly basis for the first 3 years after product approval. (See Attachment E).

C. Elements To Assure Safe Use

The REMS does not include elements to assure safe use

D. Implementation System

An implementation system is not required, since the REMS does not include elements to assure safe use.

E. Timetable for Submission of Assessments

Savient will submit REMS Assessments to the FDA at 1 year, 2 years, 3 years, 5 years and 7 years from the date of the approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Savient will submit each assessment so that it will be received by the FDA within 60 days of the due date. The due date is calculated from the date of launch or 60 days from the approval of the BLA, whichever is sooner.

Medication Guide

KRYSTEXXA™ (Phonetic spelling: Kris-TEX-a)

(pegloticase) Injection

For Intravenous Infusion

Read this Medication Guide before you start receiving KRYSTEXXA and before each treatment. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment. Talk to your doctor if you have any questions about your treatment with KRYSTEXXA.

What is the most important information I should know about KRYSTEXXA?

Serious allergic reactions may happen in some people who receive KRYSTEXXA. These allergic reactions can be life threatening and usually happen within 2 hours of the infusion.

KRYSTEXXA should be given to you by a doctor or nurse in a healthcare setting where serious allergic reactions can be treated. Your doctor or nurse should watch you for any signs of a serious allergic reaction during and after your treatment with KRYSTEXXA.

Tell your doctor or nurse right away if you have any of these symptoms during or after your treatment with KRYSTEXXA:

- wheezing, shortness of breath, cough, chest tightness, chest pain, or trouble breathing
- dizziness, fainting, fast or weak heartbeat or feeling nervous
- reddening of the face, itching, hives, or feeling warm
- swelling of the throat or tongue, throat tightness, hoarse voice or trouble swallowing

What is KRYSTEXXA?

KRYSTEXXA is a prescription medicine used in adults to help reduce the signs and symptoms of gout that are not controlled by other treatments.

People with gout have too much uric acid in their body. Uric acid crystals collect in joints, kidneys, and other organs. This may cause pain, redness and swelling (inflammation). KRYSTEXXA works to lower blood levels of uric acid.

It is not known if KRYSTEXXA is safe and effective in children.

Who should not receive KRYSTEXXA?

Do not receive KRYSTEXXA if you have a rare blood problem called glucose 6-phosphate dehydrogenase (G6PD) deficiency or favism. Your doctor may test you for G6PD before you start KRYSTEXXA.

What should I tell my doctor before receiving treatment with KRYSTEXXA?

Before you receive KRYSTEXXA, tell your doctor if you:

- know you have G6PD deficiency
- ever had any heart problems or high blood pressure
- are pregnant or plan to become pregnant. It is not known if KRYSTEXXA will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if KRYSTEXXA passes into your breast milk. You and your doctor should decide if you will receive KRYSTEXXA or breastfeed.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of your medicines and show them to your doctor and pharmacist when you get a new medicine.

How will I receive KRYSTEXXA?

- **Your doctor may give you medicine before your treatment of KRYSTEXXA to help reduce your chance of getting a reaction. Take these medicines as directed by your doctor or nurse.**
- You will receive KRYSTEXXA through a needle in your vein (i.v. infusion).
- Your treatment will take about 2 hours or sometimes longer. A doctor or nurse will give you the treatment.
- You will receive KRYSTEXXA every 2 weeks.
- If you have side effects, your doctor may stop or slow the infusion and may give you medicine to help the side effects.
- A doctor or nurse will watch you for side effects while you receive KRYSTEXXA and for some time afterwards.
- Your doctor may stop your KRYSTEXXA if your uric acid levels do not become normal and stay controlled or you have certain side effects.
- Your gout flares may increase in the first 3 months when you start receiving KRYSTEXXA. Do not stop receiving KRYSTEXXA even if you have a flare as the amount of flares will decrease after 3 months of treatment. Your doctor may give you other medicines to help reduce your gout flares for the first few months after starting KRYSTEXXA.

What are the possible side effects of KRYSTEXXA?

KRYSTEXXA may cause serious side effects. See “What is the most important information I should know about KRYSTEXXA.”

The most common side effects of KRYSTEXXA include:

- gout flares
- allergic reactions. See “What is the most important information I should know about KRYSTEXXA.”
- bruising
- sore throat
- constipation
- chest pain
- vomiting

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the side effects of KRYSTEXXA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to Savient Pharmaceuticals at 1-888-579-7839.

General information about the safe and effective use of KRYSTEXXA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about KRYSTEXXA. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about KRYSTEXXA that is written for health professionals.

For more information, go to www.KRYSTEXXA.com or www.SAVIENT.com or call 1-888-579-7839.

What are the ingredients in KRYSTEXXA?

Active ingredient: pegloticase

Inactive ingredients: disodium hydrogen phosphate dihydrate, sodium chloride, sodium dihydrogen phosphate dihydrate, and water for injection.

Product manufactured for:

Savient Pharmaceuticals, Inc.
One Tower Center Blvd, 14th Floor
East Brunswick, NJ 08816

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Code #: 1801

Issued September 2010

Last Modified: September 2010

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IMPORTANT DRUG WARNING
Regarding KRYSTEXXA™
(pegloticase)

Subject: Risk of anaphylaxis and infusion reactions, and contraindication of use of KRYSTEXXA in patients with G6PD deficiency.

<Insert date>

Dear Healthcare Provider:

The purpose of this letter is to inform you of important safety information about KRYSTEXXA™ (pegloticase), which has been approved by the US Food and Drug Administration (FDA). KRYSTEXXA™ (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated. KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

Important Information about the Risks of KRYSTEXXA

The FDA has approved KRYSTEXXA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the drug outweigh the risks of:

- **anaphylaxis,**
- **infusion reactions and**
- **contraindication of use of KRYSTEXXA in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency**

WARNING: ANAPHYLAXIS and INFUSION REACTIONS

See full prescribing information for complete boxed warning.

- **Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Patients should be pre-medicated with antihistamines and corticosteroids.**
- **Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.**

Anaphylaxis

Intravenous administration of KRYSTEXXA may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.

Anaphylaxis was reported in 6.5% of patients administered KRYSTEXXA every 2 weeks compared to none with placebo during pre-marketing controlled clinical trials. All patients received pre-treatment medication.

Infusion Reactions

Infusion Reactions were reported in 26% of patients administered KRYSTEXXA 8mg every 2 weeks and 41% administered 8 mg every 4 weeks compared to 5% of patients with placebo during pre-marketing controlled clinical trials. All patients received pre-treatment medication. The most commonly reported signs and symptoms included urticaria (11%), dyspnea (7%), erythema (6%), and flushing (6%). The risk of infusion reaction is higher in patients who have lost therapeutic response.

Key Aspects of Recommended Management

- Infusion reactions
 - Patients should receive pre-treatment medication prior to each infusion to minimize the risk of infusion reactions, including anaphylaxis.
 - Administer KRYSTEXXA in a healthcare setting prepared to manage anaphylaxis.
 - Observe patients for an appropriate period of time after administration.
- Serum uric acid
 - Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6mg/dL, particularly when 2 consecutive values above 6 mg/dL are observed. The risk of anaphylaxis and infusion reactions is higher in patients whose uric acid level increases to above 6 mg/dL.

Contraindication in patients with G6PD deficiency

Use of KRYSTEXXA is contraindicated in patients with G6PD deficiency due to the risk of hemolysis and methemoglobinemia. It is recommended that patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) be screened for G6PD deficiency prior to starting KRYSTEXXA.

Medication Guide

KRYSTEXXA has a **Medication Guide** that accompanies the Full Prescribing Information. You should review the information in the Medication Guide with your patients. Provide each patient with a Medication Guide every time you administer KRYSTEXXA to your patients as the information contained within may change over time.

Reporting Patient Adverse Events

Healthcare professionals should report all adverse events suspected to be associated with the use of KRYSTEXXA by calling 1-888-KRYSTEXXA (1-888-579-7839). Alternatively, report this information to FDA's MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), online (<https://www.accessdata.fda.gov/scripts/medwatch/>) or by mail, using the MedWatch form FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Read the accompanying FDA-approved Full Prescribing Information for KRYSTEXXA.

If you have any questions, please contact Savient Pharmaceuticals, Inc. Medical Information at 1-888-KRYSTEXXA (1-888-579-7839).

Please find enclosed the KRYSTEXXA Full Prescribing Information and Medication Guide.

Sincerely,

Medical Affairs
Savient Pharmaceuticals, Inc.

This letter has been reviewed and approved by the FDA as part of the KRYSTEXXA REMS.

This site is intended for U.S. audiences only.

[Contact Us](#) | [Savient.com](#)

KRYSTEXXA™

(pegloticase)

[Prescribing Information](#)[Medication Guide](#)[REMS](#)

Risk Evaluation and Mitigation Strategy (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

In order for Savient Pharmaceuticals, Inc. (Savient) to communicate certain risks about KRYSTEXXA™ (pegloticase), Savient has worked with the FDA to develop materials to communicate the risks of:

- Anaphylaxis
- Infusion reactions
- Contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency

The REMS program is designed to inform healthcare providers and patients about the risks with KRYSTEXXA. To learn more about serious risks, read the important safety information provided in this link, including the Medication Guide, and discuss it with your patients.

The goals of the KRYSTEXXA REMS are:

- To inform healthcare providers about anaphylaxis, infusion reactions, and contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.
- To inform patients about the serious risks associated with use of KRYSTEXXA.

Use the links below to access important REMS documents

[!\[\]\(eb1074bfd91059c9cff57cf6b5c22a5b_img.jpg\) Prescribing Information](#)[!\[\]\(e11f4c47008b23dfe2f4f7c6bb9034d1_img.jpg\) Dear Healthcare Provider Letter](#)[!\[\]\(1f22188757847a0ffb7e4386ed38dfee_img.jpg\) Medication Guide](#)[!\[\]\(8b489669e5348baffa74b0cc87030268_img.jpg\) Dear Infusion Site Medical Personnel Letter](#)[!\[\]\(cab4bf952ad41dda9681cfcbefe1a76e_img.jpg\) Medical Journal Information Piece](#)[Back to home page](#)[Privacy Notice](#) | [Terms of Use](#)

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SAVIENT
PHARMACEUTICALS, INC.

IMPORTANT DRUG WARNING
Regarding KRYSTEXXA™
(pegloticase)

Subject: Risk of anaphylaxis and infusion reactions, and contraindication of use of KRYSTEXXA in patients with G6PD deficiency.

<Insert date>

Dear Infusion Site Medical Personnel:

The purpose of this letter is to inform you of important safety information about KRYSTEXXA™ (pegloticase), which has been approved by the US Food and Drug Administration (FDA). KRYSTEXXA™ (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated. KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

Important Information about the Risks of KRYSTEXXA

The FDA has approved KRYSTEXXA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the drug outweigh the risks of:

- **anaphylaxis,**
- **infusion reactions and**
- **contraindication of use of KRYSTEXXA in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency**

WARNING: ANAPHYLAXIS and INFUSION REACTIONS

See full prescribing information for complete boxed warning.

- **Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Patients should be pre-medicated with antihistamines and corticosteroids.**
- **Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.**

Anaphylaxis

Intravenous administration of KRYSTEXXA may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.

Anaphylaxis was reported in 6.5% of patients administered KRYSTEXXA 8 mg every 2 weeks compared to none with placebo during pre-marketing controlled clinical trials. All patients received pre-treatment medication.

Infusion Reactions

Infusion Reactions were reported in 26% of patients administered KRYSTEXXA 8 mg every 2 weeks and 41% administered 8 mg every 4 weeks compared to 5% of patients with placebo during pre-marketing clinical trials. All patients received pre-treatment medication. The most commonly reported signs and symptoms included urticaria (11%), dyspnea (7%), erythema (6%), and flushing (6%). The risk of infusion reaction is higher in patients who have lost therapeutic response.

Key Aspects of Recommended Management

- Infusion reactions
 - Patients should receive pre-treatment medication prior to each infusion to minimize the risk of infusion reactions, including anaphylaxis.
 - Administer KRYSTEXXA in a healthcare setting prepared to manage anaphylaxis.
 - Observe patients for an appropriate period of time after administration.
- Serum uric acid
 - Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6mg/dL, particularly when 2 consecutive values above 6 mg/dL are observed. The risk of anaphylaxis and infusion reactions is higher in patients whose uric acid level increases to above 6 mg/dL.

Contraindication in patients with G6PD deficiency

Use of KRYSTEXXA is contraindicated in patients with G6PD deficiency due to the risk of hemolysis and methemoglobinemia. It is recommended that patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) be screened for G6PD deficiency prior to starting KRYSTEXXA.

Medication Guide

KRYSTEXXA has a **Medication Guide** that accompanies the Full Prescribing Information. You should review the information in the Medication Guide with your patients. Provide each patient with a Medication Guide every time you administer KRYSTEXXA to your patients as the information contained within may change over time.

Reporting Patient Adverse Events

Healthcare professionals should report all adverse events suspected to be associated with the use of KRYSTEXXA by calling 1-888-KRYSTEXXA (1-888-579-7839). Alternatively, report this information to FDA's MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), online (<https://www.accessdata.fda.gov/scripts/medwatch/>) or by mail, using the MedWatch form FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Read the accompanying FDA-approved Full Prescribing Information for KRYSTEXXA.

If you have any questions, please contact Savient Pharmaceuticals, Inc. Medical Information at 1-888-KRYSTEXXA (1-888-579-7839).

Please find enclosed the KRYSTEXXA Full Prescribing Information and Medication Guide.

Sincerely,

Medical Affairs
Savient Pharmaceuticals, Inc.

This letter has been reviewed and approved by the FDA as part of the KRYSTEXXA REMS.

Important Information on the Safe Use of KRYSTEXXA™ (pegloticase)

Savient Pharmaceuticals, Inc. is providing this Important Information on the Safe Use of KRYSTEXXA™ (pegloticase) as part of our commitment to the safe and appropriate use of KRYSTEXXA.

KRYSTEXXA is a PEGylated uric acid specific enzyme for administration by intravenous infusion for the treatment of chronic gout in adult patients refractory to conventional therapy.

Decisions to use KRYSTEXXA must balance the potential benefits with the potential risks of therapy based upon your patients' individual needs. Please review the key safety information below and the product labeling carefully before initiating therapy.

The US Food and Drug Administration (FDA) has approved KRYSTEXXA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the drug outweigh the risks of anaphylaxis and infusion reactions and contraindication of use of KRYSTEXXA in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

WARNING: ANAPHYLAXIS and INFUSION REACTIONS

- Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.
- KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.
- Patients should be pre-medicated with antihistamines and corticosteroids.
- Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.
- Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

Anaphylaxis

Intravenous administration of KRYSTEXXA may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.

Anaphylaxis was reported in 5% of patients administered KRYSTEXXA during premarketing clinical trials. All patients received pre-treatment medication.

Infusion Reactions

Infusion reactions were reported in 26% of patients administered KRYSTEXXA every 2 weeks during premarketing clinical trials compared to 5% of patients treated with placebo. All patients received pre-medication. The most commonly reported signs and symptoms included urticaria (11%), dyspnea (7%), erythema (6%), and flushing (6%). The risk of infusion reaction is higher in patients who have lost therapeutic response.

Key Aspects of Recommended Management

- Infusion reactions
 - Patients should receive pre-treatment medication prior to each infusion to minimize the risk of infusion reactions, including anaphylaxis.
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Contraindication in Patients with G6PD Deficiency

Use of KRYSTEXXA is contraindicated in patients with G6PD deficiency due to the risk of hemolysis and methemoglobinemia. It is recommended that patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) be screened for G6PD deficiency prior to starting KRYSTEXXA.

Additional information: Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated. KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

If you have any questions regarding KRYSTEXXA, please contact
Savient Pharmaceuticals, Inc. Medical Information at 1-888-KRYSTEXXA
(1-888-579-7839).

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KRYSTEXXA™
(pegloticase)

This journal information piece is required and approved by FDA as part of the KRYSTEXXA REMS.